PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below
International application No. PCT/GB2005/000328	International filing date *(day/month/year)* 27.01.2005
Priority date *(day/month/year)* 30.01.2004	
International Patent Classification (IPC) or both national classification and IPC G01N33/68	
Applicant PROTHERICS MOLECULAR DESIGN LIMITED	

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/GB2005/000328

10/588078

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority for the purposes of search.

3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-3,5

because:

☒ the said international application, or the said claims Nos. 1-3 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 5

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☐ paid additional fees.

   ☐ paid additional fees under protest.

   ☒ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   see separate sheet

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-4

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	-
	No:	Claims	1-4
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-4
Industrial applicability (IA)	Yes:	Claims	4
	No:	Claims	-

2. Citations and explanations

   see separate sheet

Re Item III.

The subject-matter of claims 1-3 (insofar as it also embraces a possible method of diagnosis practised on the human and animal body: "obtaining" a prion protein containing sample from said subject) can be seen as directed to a method of treatment of the human and/or animal body. No unified criteria exist in PCT for the assessment of whether such methods are industrially applicable or not. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, recognizes formulations such as "providing a sample ..." as industrially applicable.

Therefore, present claims 1-3 relate to subject-matter considered by this authority to be covered by the provisions of R. 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Art. 34(4)(a)(i) PCT).

Re Item IV.

The separate inventions/groups of inventions are:

Invention 1: claims 1-4
A assay method for detecting infectious prion protein in a sample from a mammalian subject, said method comprising the steps as listed in claim 1 and in particular being based on an antibody capable of binding to a polypeptide having the sequence as given in claim 1.

Invention 2: claim 5
Use of a iPrP binding antibody in the manufacture of a medicament for use in the treatment of human TSE.

They are not so linked as to form a single general inventive concept (Rule 13.1 PCT) for the following reasons:

Claims 1 and 5 have in common that they involve antibodies targeted against infectious

isoforms of the prion protein (iPrP). Antibodies against iPrP's are, however, well known, for example form documents D1-D3 as cited in the search report (see whole application and in particular claims). The problem adressed in claim 1 is to provide an assay method for detecting infectious prion protein in a sample from a mammalian subject, said method comprising the steps as listed in claim 1 and in particular being based on an antibody capable of binding to a polypeptide having the sequence as given in claim 1. The problem adressed in claim 5 is the use of an iPrp in the treatment of human TSE.
This analysis demonstrates that the subject-matter of the two inventions is also not linked by providing a solution to a common problem. In conclusion, neither the technical features in common to the two claims nor the problem solved by each of the two claims provides a corresponding special technical feature which establishes a single general inventive concept linking any of the two claims. Thus, the technical relationship between the subject-matter of the two claims is lacking and the requirements for unity of invention referred to in R. 13.1 PCT is not fulfilled.

Re Item V.

1 Reference is made to the following documents:

D1 : US 5 773 572 A (FISHLEIGH ET AL) 30 June 1998 (1998-06-30)
D2 : US 2002/164335 A1 (HARRIS DAVID A ET AL) 7 November 2002 (2002-11-07)
D3 : US 6 537 548 B1 (PRUSINER STANLEY B ET AL) 25 March 2003 (2003-03-25)

2 Novelty and Inventive Step

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claim 1 is not new in the sense of Article 33(2) PCT.
Document D1 discloses (the references in parentheses applying to this document) an assay method for detection of infectious prion protein in a sample from a mammalian

subject, said method comprising (claim 1 and col. 15, lines 66-67):
a) contacting said sample with an agent which serves to digest non-infectious prion protein and to partially digest infected prion protein (D1, col. 16, lines 35-47);
b) contacting the digested sample with an antibody capable of binding a ploypeptide with the sequence according to claim 1 (see claim 12 and seq. id no. 58 and col. 7, lines 42-65);
and detecting conjugates of said antibody and said polypeptide, characterised in that the detection comprises chemical, biological or biochemical amplification of a detectable species and detection of the amplified species (see e.g example 2, col. 17 and col. 19 - col. 21).

Since D1 furthermore also discloses antibodies against the Va-region (see col.2-4), claims 1-4 are not novel over D1. Should the combination of Vc-binding antibodies with Va-binding antibodies (claim 4.(i) and (ii)) be seen as the inventive concept, inventive step could only be acknowledged if advantages or surprising effects of the present invention can be shown over D1.

2.2 The subject-matter of claims 1-4 is also not novel over D2 and D3.
D2 and D3 disclose an assay method according to claim 1, in which antibodies against different Prp amino acid mutants are disclosed (D2: see claim 4 and seq. id's 5-8, D3: col. 10, lines 16-20 and abstract). All said sequences "have" the sequence referred to in claim 1. In this context, the applicant is informed that "having" is construed as "comprising". Therefore, longer sequences as disclosed in D2 and D3 also anticipate the subject-matter of claim 1.

3. Industrial Applicability

The subject-matter of claim 4 is considered to be industrially applicable according to Art. 33(4) PCT.